

Substitute for form 1449A-PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

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Sheet 1 of 7

Complete if Known

Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623
Attorney Docket Number	NB 2008.01

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number Number - Kind Code ² (if known)	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
***	1	US 3,852,266	12-03-74	Kiyonagi et al.	
<i>gpc</i>	2	US-4,247,544	01-27-81	Bergstrom, et al.	
	3	US-4,267,171	04-12-81	Bergstrom, et al.	
	4	US-4,542,210	09-17-85	Sakata et al.	
	5	US-4,668,777	05-26-87	Caruthers et al.	
	6	US-4,816,570	03-28-89	Farquhar	
	7	US-4,948,882	08-14-90	Ruth	
	8	US-4,963,263	10-16-90	Kauver	
<i>gpc</i>	9	US-4,963,533	10-16-90	De Clercq et al.	
	10	US-4975,278	12-04-90	Senter et al.	

** Duplicate: see PTO-892 for citation.

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document Country Code ³ - Number ⁴ - Kind Code ⁵ (if known)	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
<i>gpc</i>	11	DE 32 29 169 A1	02-09-84	De Clercq et al.		
	12	EP 0 311 107 A2	04-12-89	Stichting REGA VZW		
	13	EP 0 311 108A2	04-12-89	Stichting REGA VZW		
<i>gpc</i>	14	EP 0 316 592	05-24-89	Stichting REGA VZW		
***	15	GB 982 776	02-10-65	The Wellcome Foundation		
<i>gpc</i>	16	RO 88451	01-30-86	Antibiotics Enterprise, Iasi		X
	17	WO 89/05817	06-29-89	Nucleic Acid Research Institute		
	18	WO 90/03978	04-19-90	Stichting REGA VZW		
<i>gpc</i>	19	WO 91/17424	11-14-91	Vical, Inc.		

Examiner's
Signature

L. E. Crane

Date
Considered

02/22/2005

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First Named Inventor

H. Michael SHEPARD

Art Unit

Lawrence E. Crane

Examiner Name

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Attorney Docket Number

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AA	20	US-5,070,082	12-03-01	Murdock, et al. (I)	
AA	21	US-5,077,282	12-31-01	Murdock, et al. (II)	
AA	22	US-5,077,283	12-31-01	Murdock, et al. (III)	
AA	23	US-5,085,983	02-04-92	Scanlon	
AA	24	US-5,116,822	05-26-92	De Clercq et al.	
AA	25	US-5,116,827	05-26-92	Murdock, et al. (IV)	
AA	26	US-5,133,866	07-28-92	Kauver	
AA	27	US-5,137,724	08-11-92	Balzarini et al.	
AA	28	US-5,212,101	05-18-93	Moriniere et al.	
AA	29	US-5,212,201	05-18-93	Murdock, et al. (V)	

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AA	30	WO 92/19767	11-12-92	Terrapin Technologies, Inc.		
AA	31	WO 93/06120	04-01-93	University of Rochester		
AA	32	WO 94/03467	02-17-94	Institute of Organic Chemistry & Biochemistry of the Academy of Sciences of the Czech Republic, et al.		
AA	33	WO 94/22483	10-13-94	Kozak, Alexander		

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<i>See</i>	34	US-5,217,869	06-08-93	Kauver	
	35	US-5,233,031	08-03-92	Borch et al.	
	36	US-5,264,618	11-23-93	Felgner et al.	
	37	US-5,300,425	04-05-94	Kauver	
	38	US-5,338,659	08-16-94	Kauver, et al.	
	39	US-5,430,148	07-04-95	Webber, et al.	
<i>See</i>	40	US-5,433,955	07-18-95	Bredehorst et al.	
<i>XX</i>	41	US-5,457,187	10-10-96	Gmeiner et al.	
<i>See</i>	42	US-5,459,127	10-17-85	Felgner et al.	
<i>See</i>	43	US-5,516,631	05-14-96	Frisch	

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<i>See</i>	44	WO 95/01806	01-19-95	Kondratyev, A.		
<i>XX</i>	45	WO 96/08556	03-30-96	Ameroham International, Inc.		
<i>See</i>	46	WO 95/09865	04-13-95	Terrapin Technologies, Inc.		
<i>See</i>	47	WO 95/12678	05-11-95	Connors, T. et al.		
<i>XX</i>	48	WO 96/03161	02-08-96	Springer et al.		
<i>See</i>	49	WO 96/07413	04-04-96	University of Georgia Research Foundation & Yale University		

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SignatureL. E. Crane *L. E. Crane*Date
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First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
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Attorney Docket Number	NB 2008.01

U.S. PATENT DOCUMENTS

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<i>Jhe</i>	50	US-5,521,161	05-28-96	Malley et al.	
<i>Jhe</i>	51	US-5,527,900	06-18-96	Balzarini et al.	
<i>Jhe</i>	52	US-5,596,018	01-21-97	Baba et al.	
<i>Jhe</i>	53	US-5,616,564	04-01-97	Rapaport	
<i>Jhe</i>	54	US-5,627,165	05-06-97	Glazier	
	55	US-5,645,988	07-08-97	Vande Woude et al.	
	56	US-5,663,321	09-02-97	Gmeiner et al.	
	57	US-5,733,896	03-31-98	Holy et al.	
	58	US-5,798,340	08-25-98	Bischofberger et al.	
<i>Jhe</i>	59	US-5,968,910	10-19-99	Balzarini	

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<i>Jhe</i>	60	WO 96/10030	04-04-96	leis Pharmaceuticals, Inc.		
<i>Jhe</i>	61	WO 96/23506	08-08-96	Fraunhofer Society for the Promotion of Applied Research E.V.		X
<i>Jhe</i>	62	WO 96/29336	09-26-96	Medical Research Council, University College Cardiff Consultants, Inc. Rega Foundation		

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SignatureL. E. Crane *L. E. Crane*Date
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Sheet 5 of 7

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<i>See</i>	63	US-5,981,507	11-09-99	Josephson et al.	
<i>See</i>	64	US-6,057,305	05-02-00	Holy et al.	
<i>**</i>	65	US-6,245,750	06-12-01	Shepard	
<i>**</i>	66	US-6,330,161	02-16-02	Shepard et al.	
<i>**</i>	67	US-6,406,663	12-17-02	Shepard	
<i>**</i>	68	US-2001/034440	10-26-01	Shepard et al.	
<i>**</i>	69	US-2002/0147175	10-10-02	Shepard et al.	
<i>**</i>	70	US-2002/0161610	10-17-02	Shepard et al.	

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<i>See</i>	71	WO 96/33168	10-24-96	Kumiai Chemical Industry Co Ltd et al.		
<i>See</i>	72	WO 96/40088	12-19-96	Hostetter, Karl Y.		
<i>**</i>	73	WO 96/40708	12-10-06	La Jolla Pharmaceuticals, Inc.		
<i>See</i>	74	WO 96/40739	12-19-96	Terrapin Technologies, Inc.		
<i>See</i>	75	WO 97/25342	07-17-97	Terrapin Technologies, Inc.		
<i>**</i>	76	WO 97/28170	08-07-97	Fick, James & Israel, Mark		

Examiner's
SignatureL. E. Crane *LE Crane*Date
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<i>gke</i>	77	WO 97/49717	12-31-97	Balzarini et al.		
	78	WO 98/49177	11-05-98	University College Cardiff Consultants Limited		
<i>gke</i>	79	WO 99/06072	02-11-99	Boehringer Mannheim Corp.		
**	80	WO 99/08110	02-18-99	NewBiotics, Inc.		
**	81	WO 99/20741	04-20-99	Geron Corporation		
<i>gke</i>	82	WO 99/23104	05-14-99	The Government of the United States of America represented by The Secretary of Health & Human Services		
**	83	WO 99/37763	07-28-99	NewBiotics, Inc.		

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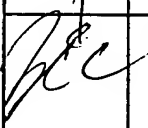
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	84	WO 00/18755	04-06-00	University College Cardiff Consultants Limited and Rega Foundation		
	85	WO 00/33888	06-15-00	Dubois, V. et al.		
	86	WO 01/07088	02-01-01	NewBiotics, Inc.		
	87	WO 01/83501	11-08-01	University College Cardiff Consultants Limited and Rega Foundation		
	88	WO 01/85749	11-15-01	University College Cardiff Consultants Limited and Rega Foundation		

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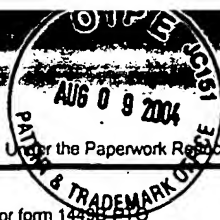
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Sheet 1 of 19

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Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623
Attorney Docket Number	NB 2008.01

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T ²
	1 !	ABRAHAM et al. "Synthesis and biological activity of aromatic amino acid phosphoramidates of 5-fluoro-2'-deoxyuridine and 1-β-arabinofuranosylcytosine: Evidence of phosphoramidase activity" <i>J. Med. Chem.</i> (1996) 39:4569-4575	
	2 !	AKDAS et al. "Glutathione S-transferase and multidrug-resistant phenotype in transitional cell carcinoma of the bladder" <i>Eur. Urol.</i> (1996) 29(4):483-486	
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Sheet 2 of 19

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Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623
Attorney Docket Number	NB 2008.01

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Jee	14	BALZARINI et al. "Mechanism of anti-HIV action of masked alaninyl d4T-MP derivatives" <i>PNAS USA</i> (July 1996) 93:7295-7299	
	15 !	BANERJEE et al. "Molecular mechanisms of resistance to antifolates, a review" <i>Acta Biochim. Pol.</i> (1995) 42(4):457-464	
	16	BANERJEE et al. "Role of E2F-1 in chemosensitivity" <i>Cancer Res.</i> (Oct. 1, 1998) 58:4292-4296	
	17 !	BARBATO et al. "Synthesis of bridged pyrimidine nucleosides and triazo [4, 3-c] pyrimidine nucleoside analogues" <i>Nucleos. Nucleot.</i> (1989) 8(4):515-528	
	18 !	BARBOUR et al. "A naturally occurring tyrosine to histidine replacement at residue 33 of human thymidylate synthase confers resistance to 5-fluoro-2'-deoxyuridine in mammalian and bacterial cells" <i>Mol. Pharmacol.</i> (1992) 42:242-248	
	19 !	BARR et al. "Reaction of 5-ethynyl-2'-deoxyuridylate with thiols and thymidylate synthetase" <i>Biochemistry</i> (1983) 22:1696-1703	
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Jee	23 !	BERTINO et al. "Resistance mechanisms to methotrexate in tumors" <i>Stem Cells</i> (1996) 14:5-9	
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Jee	25 !	BUDAVARI (July 1996) (Ed.), <i>The Merck Index</i> , 12 th Edition, Doxifluridine, page 3493	
	26 !	BUDAVARI (July 1996) (Ed.), <i>The Merck Index</i> , 12 th Edition, Floxuridine, page 4148	
	27 !	BUDAVARI (July 1996) (Ed.), <i>The Merck Index</i> , 12 th Edition, Idoxuridine, page 4934	
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	29 !	CARRERAS and SANTI "The catalytic mechanism and structure of thymidylate synthase" <i>Annu. Rev. Biochem.</i> (1995) 64:721-762	
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Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
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NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T ²
<i>He</i>	31 !	CASS et al. "Recent advances in the molecular biology of nucleoside transporters of mammalian cells" <i>Biochem. Cell Biol.</i> (1998) 76(5):761-770	
<i>He</i>	32	CATUCCI et al. "Development and significance of the HIV-1 reverse transcriptase M184V mutation during combination therapy with lamivudine, zidovudine, and protease inhibitors" <i>J. Acquir. Immune Defic. Syndr.</i> (July 1999) 21(3):203-208	
<i>He</i>	33 !	CHAUDHURI and KOOL "Very high affinity DNA recognition by bicyclic and cross-linked oligonucleotides" <i>J. Am. Chem. Soc.</i> (1995) 117:10434-10442	
<i>He</i>	34	CHEN et al. "Sensitization of human breast cancer cells to cyclophosphamide and ifosfamide by transfer of a liver cytochrome P450 gene" <i>Cancer Res.</i> (Mar. 15, 1996) 56:1331-1340	
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<i>He</i>	40 !	COPUR et al. "Thymidylate synthase gene amplification in human colon cancer cell lines resistant to 5-fluorouracil" <i>Biochem. Pharmacol.</i> (1995) 49(10):1419-1426	
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Sheet

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Application Number

10/681,418

Filing Date

October 7, 2003

First Named Inventor

H. Michael SHEPARD

Art Unit

Lawrence E. Crane

Examiner Name

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<i>JPC</i>	45	DeCLERCQ et al. "Antiviral Activity of Novel Deoxyuridine Derivatives" <u>Current Chemotherapy: Proceedings of the International Congress of Chemotherapy</u> published in <i>Virology</i> (Sept. 18, 1978) 1:352-354	
	46 !	DeCLERCQ et al. "Nucleic acid related compounds. 40. Synthesis and biological activities of 5-alkynyluracil nucleosides" <i>J. Med. Chem.</i> (1983) 26:661-666	
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Sheet 5

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<i>Me</i>	58 !	FELMINGHAM and WASHINGTON "Trends in the antimicrobial susceptibility of bacterial respiratory tract pathogens - findings of the Alexander Project 1992-1996" <i>J. Chemotherapy</i> (1999) 11(Suppl 1):5-21	
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<i>Me</i>	66 !	GRAHAM et al. "DNA duplexes stabilized by modified monomer residues: Synthesis and stability" <i>J. Chem. Soc. Perkin Trans.</i> (1998) 1:1131-1138	
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				Application Number	10/681,418
				Filing Date	October 7, 2003
				First Named Inventor	H. Michael SHEPARD
				Art Unit	Lawrence E. Crane
				Examiner Name	1623
Sheet	6	of	19	Attorney Docket Number	NB 2008.01

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T ²
***	72	HSAIG and BARDOZ "Synthesis of 5'-thymidyl bis(1-aziridinyl)phosphinates as antineoplastic agents" <i>J. Med. Chem.</i> (19810 24:887-889	
JMC	73	HUDZIAK et al. "Amplified expression of the HER2/ERBB2 oncogene induces resistance to tumor necrosis factor α in NIH 3T3 cells" <i>PNAS USA</i> (July 1988) 85:5102-5106	
	74	HUSAIN et al. "Elevation of topoisomerase I messenger RNA, protein, and catalytic activity in human tumors: Demonstration of tumor-type specificity and implications for cancer chemotherapy" <i>Cancer Research</i> (Jan. 15, 1994) 54:539-546	
	75 !	JACKMAN and CALVERT "Folate-based thymidylate synthase inhibitors as anticancer drugs" <i>Ann. Oncol.</i> (1995) 6(9):871-881	
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	80	KOBAYASHI et al. "Effect of hammerhead ribozyme against human thymidylate synthase on the cytotoxicity of thymidylate synthase inhibitors" <i>Jpn. J. Cancer Res.</i> (Nov. 1995) 86:1014-1018	
JMC	81 !	KOMAKI et al. "Difference in thymidylate synthetase activity in involved nodes compared with primary tumor in breast cancer patients" <i>Breast Cancer Res. Tr.</i> (1995) 35(2):157-162	
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JMC	83 !	KWONG et al. "Hepatitis C virus NS3/4A protease" <i>Antivir. Res.</i> (1999) 41:67-84	
JMC	84	LASIC "Doxorubicin in sterically stabilized liposomes" <i>Nature</i> (Apr. 11, 1996) 380:561-562	

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**INFORMATION DISCLOSURE
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Sheet

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19

Complete if Known

Application Number

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Filing Date

October 7, 2003

First Named Inventor

H. Michael SHEPARD

Art Unit

Lawrence E. Crane

Examiner Name

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Pre	85 !	LEE et al. "Inhibition of mouse thymidylate synthase promoter activity by the wild-type p53 tumor suppressor protein" <i>Exp. Cell Res.</i> (1997) 234:270-276	
	86	LENZ et al. "p53 and thymidylate synthase expression in untreated stage II colon cancer: associations with recurrence, survival, and site" <i>Clinical Cancer Research</i> (May 1998) 4:1227-1234	
	87 !	LEŠ et al. "Modeling of reaction steps relevant to deoxyuridylate (dUMP) enzymatic methylation and thymidylate synthase mechanism-based inhibition" <i>Journal of Biomolecular Structure & Dynamics</i> (1998) 15(4):703-715	
	88 !	LEWIS et al. "Differential responses of human tumor cell lines to anti-p185 ^{HER2} monoclonal antibodies" <i>Cancer Immunol. Immunother.</i> (1993) 37(4):255-263	
	89	LEWIS et al. "A serum-resistant cytofection for cellular delivery of antisense oligodeoxynucleotides and plasmid DNA" <i>PNAS USA.</i> (April 1996) 93:3176-3181	
	90	LIN et al., "Rhenium188 hydroxyethylidene diphosphonate: a new generator-produced radiotherapeutic drug of potential value for the treatment of bone metastases" <i>Eur. J. Nucl. Med.</i> 24(6):590-595 (June 1997)	
	91 !	LIVAK et al. "Detection of single base differences using biotinylated nucleotides with very long linker arms" <i>Nucl. Acids Res.</i> (1992) 20(18):4831-4837	
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	94 !	LOOK et al. "Increased thymidine kinase and thymidylate synthase activities in human epithelial ovarian carcinoma" <i>Anticancer Res.</i> (1997) 17:2353-2356	
	95 !	LOVEJOY et al. "Animal models and the molecular pathology of cancer" <i>J. Pathol.</i> (1997) 181:130-135	
	96 !	MADEC et al. "Some characteristics of fetal and adult isoenzymes of thymidine kinase in human breast cancers" <i>Bull. Cancer</i> (1998) 75:187-194	
	97 !	MADER et al. "Resistance to 5-fluorouracil" <i>Gen. Pharma.</i> (1998) 31(5):661-666	
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Sheet

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Application Number

10/681,418

Filing Date

October 7, 2003

First Named Inventor

H. Michael SHEPARD

Art Unit

Lawrence E. Crane

Examiner Name

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ck	100	MOINTEE "Probing the mechanism of action and decomposition of amino acid phosphomonoester amidates of antiviral nucleoside prodrugs" J. Med. Chem. (1997) 40:3323-3331	
gpc	101	MEAD et al. "Pharmacologic aspects of homofolate derivatives in relation to amethopterin-resistant murine leukemia" <i>Cancer Res.</i> (Nov. 1966) 26(1):2374-2379	
	102 !	MEIER et al. "ADA-bypass by lipophilic cyclosal-ddAMP pro-nucleotides a second example of the efficiency of the cyclosal-concept" <i>Bioorg. Med. Chem. Lett.</i> (1997) 7(12):1577-1582	
	103 !	MEIER et al. "Cyclic saligenyl phosphotriesters of 2',3'-dideoxy-2',3'-didehydrothymidine (d4T) - a new pro-nucleotide approach" <i>Bioorg. Med. Chem. Lett.</i> (1997) 7(2):99-104	
	104 !	MEIER et al. "CycloSal-pro-nucleotides: The design and biological evaluation of a new class of lipophilic nucleotide prodrugs" <i>Int'l. Antiviral News</i> (1997) 5(10):183-185	
	105 !	MELTON et al. "Antibody-directed enzyme prodrug therapy (ADEPT). Review article" <i>Drugs of the Future</i> (1996) 21(2):167-181	
	106	MELTON and SHERWOOD "Antibody-enzyme conjugates for cancer therapy" <i>J. Natl. Cancer Inst.</i> (Feb. 21, 1996) 88(3/4):153-165	
	107	MOBASHERY and JOHNSTON "Reactions of <i>Escherichia coli</i> TEM β -lactamase with cephalothin and with C ₁₀ -dipeptidyl cephalosporin esters" <i>J. Biol. Chem.</i> (June 15, 1986) 261(17):7879-7887	
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Sheet

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19

Complete if Known

Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623
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JEC	116 !	PALMER et al. "Highly drug-resistant HIV-1 clinical isolates are cross-resistant to many antiretroviral compounds in current clinical development" <i>AIDS</i> (1999) 13(6):661-667	
	117 !	PARADISO et al. "Thymidilate synthase and p53 primary tumour expression as predictive factors for advanced colorectal cancer patients" <i>Brit. J. Cancer</i> (2000) 82(3):560-567	
	118	PATTERSON et al. "Thymidine phosphorylase moderates thymidine-dependent rescue after exposure to the thymidylate synthase inhibitor ZD1694 (tomudex) <i>in vitro</i> " <i>Cancer Res.</i> (July 1, 1998) 58:2737-2740	
	119 !	PEDERSEN-LANE et al. "High-level expression of human thymidylate synthase" <i>Protein Expression and Purification</i> (1997) 10:256-262	
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	122 !	PHELPS et al. "Synthesis and biological activity of 5-fluoro-2'-deoxyuridine 5'-phosphorodiamidates" <i>J. Med. Chem.</i> (1980) 23:1229-1232	
JEC	123	PLUTA et al., "Synthesis and biological properties of 4-hydroxy, 4-thio-5-pyrimidine derivatives" <i>Boll. Chim. Farmaceutico</i> (Gennaio 1999) 138(1):30-33	
*8	124	ROBINS and BARR "Nucleic acid related compounds. 34. Smooth and efficient palladium-copper catalyzed coupling of terminal alkynes with 5-iodouracil nucleosides" <i>Tetrahedron Lett.</i> (1981) 22:421-424	
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Sheet 10 of 19

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Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
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Examiner Name	1623
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	130	RUTH and BERGSTRÖM "C-5 substituted pyrimidine nucleosides. 1. Synthesis of C-5 allyl, propyl, and propenyl uracil and cytosine nucleosides via organopalladium intermediates" J. Org. Chem. (1978) 43(14):2870-2876	
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	132	SANTI "Perspectives on the design and biochemical pharmacology of inhibitors of thymidylate synthetase" <i>J. Med. Chem.</i> (Feb. 1980) 23(2):103-111	
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Sheet 11

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First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623
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<i>[Signature]</i>	145 !	TEH et al. "Tumor suppressor genes (TSG)" <i>Anticancer Research</i> (1999) 19:4715-4728	
	146 !	TOLSTIKOV et al. "Synthesis and DNA duplex stabilities of oligonucleotides containing C-5-(3-methoxypropynyl)-2'-deoxyuridine residues" <i>Nucleos. Nucleot.</i> (1997) 16(3):215-225	
	147	TOUROTOGLOU and PAZDAR "Thymidylate synthase inhibitors" <i>Clin. Cancer Res.</i> (Feb. 1996) 2(2):227-243	
	148 !	TROUTNER "Chemical and physical properties of radionuclides" <i>Nucl. Med. Biol.</i> (1987) 14(3):171-176	
	149 !	TURNER and SUMMERS "Structural biology of HIV" <i>J. Mol. Biol.</i> (1999) 285:1-32	
	150 !	VALETTE et al. "Decomposition pathways and <i>in vitro</i> HIV inhibitory effects of isodda pronucleotides: Toward a rational approach for intracellular delivery of nucleoside 5'-monophosphates" <i>J. Med. Chem.</i> (1996) 39:1981-1990	
	151	van LAAR "Therapeutic efficacy of fluoropyrimidines depends on the duration of thymidylate synthase inhibition in the murine colon 26-B carcinoma tumor model" <i>Clin. Cancer Res.</i> (Aug. 1996) 2(8):1327-1333	
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Sheet 12 of 19

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Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623
Attorney Docket Number	NB 2008.01

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T ²
<i>McC</i>	159!	WHALEN and BOYER "Human glutathione S-transferases" <i>Seminars in Liver Disease</i> (1998) 18(4):345-358	
	160!	WILDNER et al. "Enzyme prodrug gene therapy: Synergistic use of the herpes simplex virus-cellular thymidine kinase/ganciclovir system and thymidylate synthase inhibitors for the treatment of colon cancer" <i>Cancer Res.</i> (Oct. 15, 1999) 59(20):5233-5238	
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Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
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<i>Mc</i>	171 !	BARR et al. "Thymidylate synthetase-catalyzed conversions of E-5-(2-bromovinyl)-2'-deoxyuridylate" <i>J. Biol. Chem.</i> (1983) 258(22):13627-13631	
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Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623
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NON PATENT LITERATURE DOCUMENTS

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<i>He</i>	186	DAVISSON et al. "Expression of human thymidylate synthase in <i>Escherichia coli</i> . (Additions and corrections)" <i>J. Biol. Chem.</i> (Dec. 2, 1994) 269(48):30740	
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<i>He</i>	190 !	EISENBRAND et al. "An approach towards more selective anticancer agents" <i>J. Synthetic Organic Chem.</i> (1996) 10:1246-1258	
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<i>He</i>	192 !	EVARD et al. "An in vitro nucleoside analog screening method for cancer gene therapy" <i>Chem. Abstracts</i> (1996) 126:Abstract No. 26514	
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First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623
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<i>See</i>	201	GROS et al. "Isolation and expression of a complementary DNA that confers multidrug resistance" <i>Nature</i> (Oct. 1986) 323:728-731	
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<i>See</i>	204 !	GUDKOV et al. "Cloning and characterization of DNA sequences amplified in multidrug-resistant djungarian hamster and mouse cells" <i>Somat. Cell Mol. Genet.</i> (1987) 13(6):609-619	
xx	205	HAKIMELAH et al. "Design, synthesis and structure-activity relationship of novel dinucleotide analogs as agents against herpes and human immunodeficiency viruses" <i>J. Med. Chem.</i> (Nov. 10, 1995) 38(23):4648-4659	
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[Signature]	215 !	HUSAK et al. "Pseudotumour of the tongue caused by herpes simplex virus type 2 in an HIV-1 infected immunosuppressed patient" <i>Brit. J. Dermatol.</i> (1998) 139:118-121	
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Application Number

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Filing Date

October 7, 2003

First Named Inventor

H. Michael SHEPARD

Art Unit

Lawrence E. Crane

Examiner Name

1623

Attorney Docket Number

NB 2008.01

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T ²
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Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623
Attorney Docket Number	NB 2008.01

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T ²
<i>He</i>	245 !	NOOTER and STOTER "Molecular mechanisms of multidrug resistance in cancer chemotherapy" <i>Path. Res. Pract.</i> (1996) 192:768-780	
<i>He</i>	246 !	OSAKI et al. "5-fluorouracil (5-FU) induced apoptosis in gastric cancer cell lines: Role of the p53 gene" <i>Apoptosis</i> (1997) 2:221-226	
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Art Unit

Lawrence E. Crane

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<i>He</i>	263	SNYDMAN et al. "Analysis of trends in antimicrobial resistance patterns among clinical isolates of <i>Bacteroides fragilis</i> group species from 1990 to 1994" <i>Clin. Infect. Dis.</i> (1996) 23(Suppl. 1):S54-S65	
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